# Clinical trial results:
# Randomized, multicenter, double-blind, placebo-controlled, parallel-group phase III study to investigate the efficacy, safety, and tolerability of 2 different doses of IgPro20 (subcutaneous immunoglobulin) for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) – the PATH study

## Summary

| | |
|---|---|
| EudraCT number | 2011-003448-28 |
| Trial protocol | DE CZ ES FI NL AT GB IT BE LT PL EE |
| Global end of trial date | 20 September 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 October 2017 |
| First version publication date | 14 October 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | IgPro20_3003 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01545076 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | CSL Behring GmbH |
| Sponsor organisation address | Emil-von-Behring-Strasse 76, Marburg, Germany, |
| Public contact | Trial Disclosure Manager, CSL Behring GmbH, clinicaltrials@cslbehring.com |
| Scientific contact | Trial Disclosure Manager, CSL Behring GmbH, clinicaltrials@cslbehring.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 10 November 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 September 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 September 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To determine the efficacy of 2 different doses of IgPro20 (0.2 g/kg bw and/or 0.4 g/kg bw) in the maintenance treatment of CIDP in comparison to placebo.

Protection of trial subjects:

This study was carried out in accordance with the ICH (International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human
Use) Good Clinical Practice (GCP) guidelines, the Declaration of Helsinki (version 2008), and standard operating procedures for clinical research and development at CSL Behring GmbH and the Contract Research Organizations (CROs) involved.

The study was conducted under a protocol reviewed and approved by an IEC / IRB; the study was conducted by scientifically and medically qualified persons; the benefits of the study were in proportion to the risks; the rights and welfare of the subjects were respected; the physicians conducting the study did not find the hazards to outweigh the potential benefits; the results reported are accurate, and each subject or subject's legal guardian gave his or her written informed consent before any protocol-driven tests or evaluations were performed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 12 March 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Netherlands: 10 |
| Country: Number of subjects enrolled | Poland: 10 |
| Country: Number of subjects enrolled | Spain: 21 |
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Country: Number of subjects enrolled | Belgium: 2 |
| Country: Number of subjects enrolled | Czech Republic: 7 |
| Country: Number of subjects enrolled | Estonia: 3 |
| Country: Number of subjects enrolled | Finland: 1 |
| Country: Number of subjects enrolled | France: 13 |
| Country: Number of subjects enrolled | Germany: 65 |
| Country: Number of subjects enrolled | Italy: 41 |
| Country: Number of subjects enrolled | Australia: 8 |
| Country: Number of subjects enrolled | Canada: 25 |
| Country: Number of subjects enrolled | Israel: 4 |

| | |
|---|---|
| Country: Number of subjects enrolled | Japan: 17 |
| Country: Number of subjects enrolled | United States: 42 |
| Worldwide total number of subjects | 276 |
| EEA total number of subjects | 180 |

Notes:

**Subjects enrolled per age group**

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 191 |
| From 65 to 84 years | 85 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Of the 276 subjects screened, 31 were found not eligible. Therefore, 245 eligible subjects with CIDP entered the IgG Dependency Period during which time no IVIG was administered. Out of these, 208 subjects who experienced CIDP deterioration during the IgG Dependency Period qualified for the IgPro10 Restabilization Period.

### Period 1

| | |
|---|---|
| Period 1 title | IgPro10 Restabilization |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | IgPro10 |

Arm description:

Subjects who experienced CIDP deterioration during the IgG Dependency Period started up to 13 weeks of IVIG treatment with IgPro10 during the IgPro10 Restabilization Period. Of the 208 subjects that started this period, 207 received IgPro10.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IgPro10 |
| Investigational medicinal product code | |
| Other name | Privigen |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IgPro10 as 1 loading dose of 2 g/kg bw, followed by 3 or 4 maintenance doses (depending on time needed for restabilization) of 1 g/kg bw every 3 weeks.

| **Number of subjects in period 1** | IgPro10 |
|---|---|
| Started | 208 |
| Completed | 172 |
| Not completed | 36 |
| Consent withdrawn by subject | 7 |
| Physician decision | 2 |
| Failure to meet randomization criteria | 22 |
| Adverse event, non-fatal | 4 |
| Protocol deviation | 1 |

## Period 2

| | |
|---|---|
| Period 2 title | IgPro20 Subcutaneous (SC) Treatment |
| Is this the baseline period? | Yes[1] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor, Data analyst |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | IgPro20 (0.2) |

Arm description:

IgPro20 at a dose of 0.2 g/kg bw

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IgPro20 |
| Investigational medicinal product code | |
| Other name | Hizentra |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Weekly subcutaneous (SC) infusion of IgPro20 at 0.2 g/kg bw for up to 24 weeks.

| | |
|---|---|
| **Arm title** | IgPro20 (0.4) |

Arm description:

IgPro20 at a dose of 0.4 g/kg bw

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IgPro20 |
| Investigational medicinal product code | |
| Other name | Hizentra |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Weekly subcutaneous (SC) infusion of IgPro20 at 0.4 g/kg bw for up to 24 weeks.

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

2% human albumin solution

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Weekly SC infusion for up to 24 weeks.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The study was designed for IgPro20 SC randomization, therefore this is the subject population that should be used as the baseline.

| **Number of subjects in period 2[2]** | IgPro20 (0.2) | IgPro20 (0.4) | Placebo |
|---|---|---|---|
| Started | 57 | 58 | 57 |
| Completed | 36 | 39 | 21 |
| Not completed | 21 | 19 | 36 |
| Consent withdrawn by subject | 2 | 8 | 3 |
| Physician decision | - | - | 1 |
| Adverse event, non-fatal | 1 | 1 | - |
| Lack of efficacy | 18 | 10 | 32 |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The study was designed for IgPro20 SC randomization, therefore this is the subject population that should be used as the baseline.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | IgPro20 (0.2) |
| Reporting group description:<br>IgPro20 at a dose of 0.2 g/kg bw | |
| Reporting group title | IgPro20 (0.4) |
| Reporting group description:<br>IgPro20 at a dose of 0.4 g/kg bw | |
| Reporting group title | Placebo |
| Reporting group description:<br>2% human albumin solution | |

| Reporting group values | IgPro20 (0.2) | IgPro20 (0.4) | Placebo |
|---|---|---|---|
| Number of subjects | 57 | 58 | 57 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 41 | 40 | 41 |
| From 65-84 years | 16 | 18 | 16 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 57.5 | 56.6 | 55.9 |
| standard deviation | ± 12.02 | ± 13.62 | ± 12.64 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 15 | 27 | 20 |
| Male | 42 | 31 | 37 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 172 | | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 122 | | |
| From 65-84 years | 50 | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 62 | | |
| Male | 110 | | |

## End points reporting groups

| | |
|---|---|
| Reporting group title | IgPro10 |
| Reporting group description: | |
| Subjects who experienced CIDP deterioration during the IgG Dependency Period started up to 13 weeks of IVIG treatment with IgPro10 during the IgPro10 Restabilization Period. Of the 208 subjects that started this period, 207 received IgPro10. | |
| Reporting group title | IgPro20 (0.2) |
| Reporting group description: | |
| IgPro20 at a dose of 0.2 g/kg bw | |
| Reporting group title | IgPro20 (0.4) |
| Reporting group description: | |
| IgPro20 at a dose of 0.4 g/kg bw | |
| Reporting group title | Placebo |
| Reporting group description: | |
| 2% human albumin solution | |
| Subject analysis set title | ITTS |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Intention-to-treat Set (ITTS): The ITTS consists of all randomized subjects who received at least 1 dose of IgPro20 / placebo and satisfied inclusion criterion #1 (diagnosis of CIDP). | |
| Subject analysis set title | SDS |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Safety Data Set (SDS): The SDS consists of all randomized subjects who received at least 1 dose of IgPro20 or placebo. | |
| Subject analysis set title | PSDS |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Pre-randomization Safety Data Set (PSDS): The PSDS was based on all subjects enrolled into the study who received at least 1 dose of IgPro10 before randomization. | |
| Subject analysis set title | RSDS |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Rescue Medication Safety Data Set (RSDS): The RSDS consists of subjects of the SDS who received at least 1 dose of IgPro10 rescue medication. | |

## Primary: Percentage (%) of subjects who relapse or are withdrawn for any other reason during the SC treatment period (ITTS)

| | |
|---|---|
| End point title | Percentage (%) of subjects who relapse or are withdrawn for any other reason during the SC treatment period (ITTS) |
| End point description: | |
| Relapse is defined as an increase of at least 1 INCAT score point (except for the increase from 0 to 1 in the upper limb score). The INCAT score is a 10-point scale that covers the functionality of legs and arms, and has been successfully used to measure treatment effects in various CIDP studies. Scores for arm disability range from 0 (“No upper limb problems”) to 5 (“Inability to use either arm for any purposeful movement”), and scores for leg disability range from 0 (“Walking not affected”) to 5 (“Restricted to wheelchair, unable to stand and walk a few steps with help”). The INCAT (total) score is the sum of these 2 scores and ranges from 0 to 10. For the “adjusted” INCAT score, changes in the function of the upper limbs from 0 (normal) to 1 (minor symptoms) or from 1 to 0 were not recorded as deterioration or improvement because these changes are not considered clinically significant. | |
| End point type | Primary |

| End point timeframe: |
|---|
| Up to 25 weeks |

| **End point values** | IgPro20 (0.2) | IgPro20 (0.4) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 57 | |
| Units: Percent of subjects | | | | |
| number (not applicable) | 38.6 | 32.8 | 63.2 | |

**Statistical analyses**

| **Statistical analysis title** | CIDP Relapse or Withdrawal (IgPro20, 0.2) |
|---|---|
| Comparison groups | IgPro20 (0.2) v Placebo |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.007 |
| Method | Fisher exact |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -24.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -40.7 |
| upper limit | -6.21 |

| **Statistical analysis title** | CIDP Relapse or Withdrawal (IgPro20, 0.4) |
|---|---|
| Comparison groups | IgPro20 (0.4) v Placebo |
| Number of subjects included in analysis | 115 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Fisher exact |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -30.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -46 |
| upper limit | -12.2 |

## Secondary: Change from baseline in Inflammatory Neuropathy Cause and Treatment (INCAT) total scores during the SC treatment period (ITTS)

| End point title | Change from baseline in Inflammatory Neuropathy Cause and Treatment (INCAT) total scores during the SC treatment period (ITTS) |
|---|---|

End point description:

The INCAT score is a 10-point scale that covers the functionality of legs and arms, and has been successfully used to measure treatment effects in various CIDP studies. Scores for arm disability range from 0 (“No upper limb problems”) to 5 (“Inability to use either arm for any purposeful movement”), and scores for leg disability range from 0 (“Walking not affected”) to 5 (“Restricted to wheelchair, unable to stand and walk a few steps with help”). The INCAT (total) score is the sum of these 2 scores and ranges from 0 to 10. For the “adjusted” INCAT score, changes in the function of the upper limbs from 0 (normal) to 1 (minor symptoms) or from 1 to 0 were not recorded as deterioration or improvement because these changes are not considered clinically significant.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and up to 25 weeks

| **End point values** | IgPro20 (0.2) | IgPro20 (0.4) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 57 | 57 | |
| Units: Scores on scale | | | | |
| median (full range (min-max)) | 0 (-2 to 5) | 0 (-2 to 3) | 1 (-1 to 4) | |

### Statistical analyses

| **Statistical analysis title** | Median difference from Baseline (IgPro20, 0.2) |
|---|---|
| Comparison groups | IgPro20 (0.2) v Placebo |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.005 |
| Method | Wilcoxon rank sum |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 0 |

| **Statistical analysis title** | Median difference from Baseline (IgPro20, 0.4) |
|---|---|
| Comparison groups | IgPro20 (0.4) v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Wilcoxon rank sum |
| Parameter estimate | Median difference (final values) |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 0 |

## Secondary: Change from baseline in mean grip strength during the SC treatment period (ITTS)

| | |
|---|---|
| End point title | Change from baseline in mean grip strength during the SC treatment period (ITTS) |

End point description:

The hand-held Vigorimeter is a device that measures the strength of small muscles in the hand; ie, grip strength. Subjects squeezed a rubber bulb lying between the palm of the hand and the thumb and index fingers. The pressure was recorded via a rubber tube on a nanometer and expressed in kilopascal. At each assessment, the
subjects squeezed 3 times with each hand. The mean grip strength of each hand was determined.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline and up to 25 weeks

| End point values | IgPro20 (0.2) | IgPro20 (0.4) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 57 | 57 | |
| Units: Kilopascal (kPa) | | | | |
| median (full range (min-max)) | -0.6 (-80 to 55) | -2.7 (-80 to 55) | -6.6 (-51 to 22) | |

### Statistical analyses

| Statistical analysis title | Median difference from Baseline (IgPro20, 0.2) |
|---|---|
| Comparison groups | IgPro20 (0.2) v Placebo |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.004 |
| Method | Wilcoxon rank sum |
| Parameter estimate | Median difference (final values) |
| Point estimate | 7.6 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2 |
| upper limit | 14 |

| | |
|---|---|
| **Statistical analysis title** | Median difference from Baseline (IgPro20, 0.4) |
| Comparison groups | Placebo v IgPro20 (0.4) |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.014 |
| Method | Wilcoxon rank sum |
| Parameter estimate | Median difference (final values) |
| Point estimate | 5.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 11.7 |

**Secondary: Change from baseline in Medical Research Council (MRC) sum scores during the SC treatment period (ITTS)**

| | |
|---|---|
| End point title | Change from baseline in Medical Research Council (MRC) sum scores during the SC treatment period (ITTS) |

End point description:

An adapted version of the MRC sum score was used in the study. The MRC sum score is the sum of all 16 muscle scores, and ranges from 0 (paralysis) to 80 (normal strength).

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline and up to 25 weeks

| **End point values** | IgPro20 (0.2) | IgPro20 (0.4) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 56 | 57 | 57 | |
| Units: scores on a scale | | | | |
| median (full range (min-max)) | 0 (-16 to 14) | 0 (-12 to 7) | -2 (-19 to 6) | |

**Statistical analyses**

| **Statistical analysis title** | Median difference from baseline (IgPro20, 0.2) |
|---|---|
| Comparison groups | Placebo v IgPro20 (0.2) |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.003 |
| Method | Wilcoxon rank sum |
| Parameter estimate | Median difference (final values) |
| Point estimate | 2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 4 |

| **Statistical analysis title** | Median difference from baseline (IgPro20, 0.4) |
|---|---|
| Comparison groups | Placebo v IgPro20 (0.4) |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.002 |
| Method | Wilcoxon rank sum |
| Parameter estimate | Median difference (final values) |
| Point estimate | 2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 4 |

## Secondary: Change from baseline in Rasch-built Overall Disability Scale (R-ODS) scores during the SC Treatment Period (ITTS)

| End point title | Change from baseline in Rasch-built Overall Disability Scale (R-ODS) scores during the SC Treatment Period (ITTS) |
|---|---|

End point description:

The R-ODS centile score captures activity and social participation in subjects with CIDP. The R-ODS centile score ranges from 0 (most severe activity and social participation limitations) to 100 (no activity and social participation limitations).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and up to 25 weeks

| End point values | IgPro20 (0.2) | IgPro20 (0.4) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 53 | 53 | 52 | |
| Units: scores on a scale | | | | |
| median (full range (min-max)) | -2 (-41 to 100) | 0 (-49 to 17) | -3 (-43 to 13) | |

**Statistical analyses**

| Statistical analysis title | Median difference from Baseline (IgPro20, 0.2) |
|---|---|
| Comparison groups | IgPro20 (0.2) v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.03 |
| Method | Wilcoxon rank sum |
| Parameter estimate | Median difference (final values) |
| Point estimate | 3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 9 |

| Statistical analysis title | Median difference from Baseline (IgPro20, 0.4) |
|---|---|
| Comparison groups | IgPro20 (0.4) v Placebo |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Wilcoxon rank sum |
| Parameter estimate | Median difference (final values) |
| Point estimate | 5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2 |
| upper limit | 9 |

**Secondary: Rate of adverse events per IgPro20 infusion during the SC treatment period (SDS)**

| End point title | Rate of adverse events per IgPro20 infusion during the SC treatment period (SDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 28 weeks

| **End point values** | IgPro20 (0.2) | IgPro20 (0.4) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 57 | |
| Units: Rate/Infusion | | | | |
| number (not applicable) | 0.079 | 0.051 | 0.034 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with adverse events during the SC Treatment Period (SDS)

| End point title | Number of subjects with adverse events during the SC Treatment Period (SDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 28 weeks

| **End point values** | IgPro20 (0.2) | IgPro20 (0.4) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 57 | |
| Units: Subjects | | | | |
| number (not applicable) | 33 | 30 | 21 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with adverse events during the SC Treatment Period (SDS)

| End point title | Percentage of subjects with adverse events during the SC Treatment Period (SDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 28 weeks

| End point values | IgPro20 (0.2) | IgPro20 (0.4) | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 57 | 58 | 57 | |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 57.9 | 51.7 | 36.8 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to improvement during IgPro10 Re-stabilization Therapy (PSDS)

| End point title | Time to improvement during IgPro10 Re-stabilization Therapy (PSDS) |
|---|---|

End point description:

Improvement is defined as an INCAT score decrease by 1 point (except for the decrease from 1 to 0 in the upper limb score), R-ODS improvement by at least 4 points, or Mean Grip strength improvement by at least 8 kPa in one hand.

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 207 | | | |
| Units: Days | | | | |
| median (confidence interval 95%) | 23 (22 to 23) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change in mean grip strength during IgPro10 Re-stabilization Therapy (PSDS)

| End point title | Change in mean grip strength during IgPro10 Re-stabilization Therapy (PSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Reference Visit and up to 13 weeks

| **End point values** | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 202 | | | |
| Units: kPa | | | | |
| arithmetic mean (standard deviation) | 11.27 (± 16.89) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in MRC sum score during IgPro10 Re-stabilization Therapy (PSDS)

| End point title | Change in MRC sum score during IgPro10 Re-stabilization Therapy (PSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Reference Visit and up to 13 weeks

| **End point values** | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 203 | | | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard deviation) | 3.4 (± 4.9) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in R-ODS during IgPro10 Re-stabilization Therapy (PSDS)

| End point title | Change in R-ODS during IgPro10 Re-stabilization Therapy (PSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:
Reference Visit and up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 166 | | | |
| Units: Scores on acale | | | | |
| arithmetic mean (standard deviation) | 4.7 (± 14.14) | | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change in INCAT during IgPro10 Re-stabilization Therapy (PSDS)**

| End point title | Change in INCAT during IgPro10 Re-stabilization Therapy (PSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:
Reference Visit and up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 205 | | | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard deviation) | -1.1 (± 1.2) | | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Rate of adverse events per IgPro10 infusion during Re-stabilization Therapy (PSDS)**

| End point title | Rate of adverse events per IgPro10 infusion during Re-stabilization Therapy (PSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:
Up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 207 | | | |
| Units: Rate/Infusion | | | | |
| number (not applicable) | 0.175 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with adverse events during IgPro10 Re-stabilization Therapy (PSDS)

| End point title | Number of subjects with adverse events during IgPro10 Re-stabilization Therapy (PSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 207 | | | |
| Units: Subjects | | | | |
| number (not applicable) | 100 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent of subjects with adverse events during IgPro10 Re-stabilization Therapy (PSDS)

| End point title | Percent of subjects with adverse events during IgPro10 Re-stabilization Therapy (PSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 207 | | | |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 48.3 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in mean grip strength during IgPro10 Rescue Therapy (RSDS)

| End point title | Change in mean grip strength during IgPro10 Rescue Therapy (RSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Before first rescue IgPro10 infusion and up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 35 | | | |
| Units: kPa | | | | |
| arithmetic mean (standard deviation) | 16.3 (± 17.58) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in MRC sum score during IgPro10 Rescue Therapy (RSDS)

| End point title | Change in MRC sum score during IgPro10 Rescue Therapy (RSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Before first rescue IgPro10 infusion and up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 35 | | | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard deviation) | 6.8 (± 5.28) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in R-ODS during IgPro10 Rescue Therapy (RSDS)

| End point title | Change in R-ODS during IgPro10 Rescue Therapy (RSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Before first rescue IgPro10 infusion and up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 29 | | | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard deviation) | 14 (± 14.69) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in INCAT during IgPro10 Rescue Therapy (RSDS)

| End point title | Change in INCAT during IgPro10 Rescue Therapy (RSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Before first rescue IgPro10 infusion and up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45 | | | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard deviation) | -1.3 (± 1.31) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to improvement after CIDP relapse during IgPro10 Rescue Therapy (RSDS)

| End point title | Time to improvement after CIDP relapse during IgPro10 Rescue Therapy (RSDS) |
|---|---|

End point description:

Improvement is defined as a decrease in INCAT score (except for the decrease from 1 to 0 in the upper limb score) back to or below the baseline score

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: Days | | | | |
| median (confidence interval 95%) | 23 (22 to 49) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Rate of adverse events per IgPro10 infusion during Rescue Therapy (RSDS)

| End point title | Rate of adverse events per IgPro10 infusion during Rescue Therapy (RSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: Rate/Infusion | | | | |
| number (not applicable) | 0.142 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with adverse events during IgPro10 Rescue Therapy (RSDS)

| End point title | Number of subjects with adverse events during IgPro10 Rescue Therapy (RSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: Subjects | | | | |
| number (not applicable) | 17 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent of subjects with adverse events during IgPro10 Rescue Therapy (RSDS)

| End point title | Percent of subjects with adverse events during IgPro10 Rescue Therapy (RSDS) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 weeks

| End point values | IgPro10 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 28.3 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: 4.5 years | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 14.1 |
| **Reporting groups** | |
| Reporting group title | IgPro10 Restabilization |
| Reporting group description: PSDS | |
| Reporting group title | IgPro20 (0.2) |
| Reporting group description: SDS | |
| Reporting group title | IgPro20 (0.4) |
| Reporting group description: SDS | |
| Reporting group title | Placebo |
| Reporting group description: SDS | |
| Reporting group title | IgPro10 Rescue |
| Reporting group description: RSDS | |

| Serious adverse events | IgPro10 Restabilization | IgPro20 (0.2) | IgPro20 (0.4) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 207 (5.31%) | 3 / 57 (5.26%) | 2 / 58 (3.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| Blood pressure diastolic increased | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Cardiac disorders | | | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic inflammatory demyelinating polyradiculoneuropathy | | | |
| subjects affected / exposed | 2 / 207 (0.97%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 1 / 58 (1.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 1 / 58 (1.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 57 (0.00%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 1 / 57 (1.75%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 1 / 58 (1.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 1 / 57 (1.75%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture nonunion | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 1 / 57 (1.75%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 1 / 58 (1.72%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 1 / 57 (1.75%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 1 / 57 (1.75%) | 0 / 58 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Placebo | IgPro10 Rescue | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 2 / 60 (3.33%) | |
| number of deaths (all causes) | 0 | 0 | |

| | | | |
|---|---|---|---|
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| Blood pressure diastolic increased | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic inflammatory demyelinating polyradiculoneuropathy | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemia | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture nonunion | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | IgPro10 Restabilization | IgPro20 (0.2) | IgPro20 (0.4) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 50 / 207 (24.15%) | 22 / 57 (38.60%) | 20 / 58 (34.48%) |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 5 / 207 (2.42%) | 3 / 57 (5.26%) | 1 / 58 (1.72%) |
| occurrences (all) | 5 | 8 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 34 / 207 (16.43%) | 4 / 57 (7.02%) | 4 / 58 (6.90%) |
| occurrences (all) | 53 | 5 | 4 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 207 (2.42%) | 5 / 57 (8.77%) | 0 / 58 (0.00%) |
| occurrences (all) | 11 | 5 | 0 |
| Infusion site erythema | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 5 / 57 (8.77%) | 10 / 58 (17.24%) |
| occurrences (all) | 0 | 11 | 28 |
| Infusion site swelling | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 5 / 57 (8.77%) | 6 / 58 (10.34%) |
| occurrences (all) | 0 | 8 | 8 |
| Infusion site induration | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 2 / 57 (3.51%) | 3 / 58 (5.17%) |
| occurrences (all) | 0 | 10 | 3 |

| | | | |
|---|---|---|---|
| Infusion site pain | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 3 / 57 (5.26%) | 2 / 58 (3.45%) |
| occurrences (all) | 0 | 15 | 2 |
| Infusion site warmth | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 57 (0.00%) | 3 / 58 (5.17%) |
| occurrences (all) | 0 | 0 | 3 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 10 / 207 (4.83%) | 0 / 57 (0.00%) | 1 / 58 (1.72%) |
| occurrences (all) | 12 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 3 / 207 (1.45%) | 1 / 57 (1.75%) | 3 / 58 (5.17%) |
| occurrences (all) | 3 | 1 | 3 |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 207 (1.45%) | 3 / 57 (5.26%) | 1 / 58 (1.72%) |
| occurrences (all) | 3 | 3 | 1 |
| Back pain | | | |
| subjects affected / exposed | 5 / 207 (2.42%) | 3 / 57 (5.26%) | 1 / 58 (1.72%) |
| occurrences (all) | 5 | 4 | 1 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 12 / 207 (5.80%) | 4 / 57 (7.02%) | 2 / 58 (3.45%) |
| occurrences (all) | 12 | 6 | 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 1 / 57 (1.75%) | 0 / 58 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 207 (0.97%) | 3 / 57 (5.26%) | 2 / 58 (3.45%) |
| occurrences (all) | 2 | 3 | 2 |

| **Non-serious adverse events** | Placebo | IgPro10 Rescue | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 15 / 57 (26.32%) | 7 / 60 (11.67%) | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Fall | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 57 (3.51%) | 4 / 60 (6.67%) | |
| occurrences (all) | 2 | 6 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 0 / 60 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infusion site erythema | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Infusion site swelling | | | |
| subjects affected / exposed | 2 / 57 (3.51%) | 0 / 60 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Infusion site induration | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 0 / 60 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infusion site pain | | | |
| subjects affected / exposed | 2 / 57 (3.51%) | 0 / 60 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Infusion site warmth | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 57 (3.51%) | 4 / 60 (6.67%) | |
| occurrences (all) | 2 | 4 | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 0 / 60 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Arthralgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 57 (1.75%) | 0 / 60 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 1 / 60 (1.67%) | |
| occurrences (all) | 1 | 1 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | 1 / 60 (1.67%) | |
| occurrences (all) | 1 | 1 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 57 (5.26%) | 0 / 60 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 57 (3.51%) | 0 / 60 (0.00%) | |
| occurrences (all) | 2 | 0 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 17 November 2011 | -Updated with regard to measurements and information on the occurrence of hemolysis<br>-Changes in timing of SC treatment: allowed to be performed on 1 or 2 consecutive days each study week<br>-A change in dosing for loading and rescue with IVIG: a total dose of ≤ 200 g was to be administered for subjects with a body weight greater than 100 kg |
| 12 April 2013 | -'IVIG Withdrawal Period' was changed to the 'IgG Dependency Test Period'. Daily self-assessments (R-ODS score and grip strength) were added to prove subjects´ ongoing need for IVIG<br>-The schedule and loading / maintenance dosing for the IgPro10 Rescue Period was revised to match the IgPro10 Restabilization Period. The dosing was continued until the I-NCAT score was back to the result at the Rescue Reference Visit<br>-Additional safety assessment at 4 weeks after final administration of IgPro20<br>-Addition of laboratory parameters (blood urea nitrogen, gamma-glutamyltransferase) |
| 11 September 2014 | -Number of SC infusion sites in parallel no longer specified, focus on maximum rate and volume per site allowed per protocol; volume per infusion site increased to 50 mL<br>-Addition of new post-marketing adverse reactions and precautions for IgPro20 (Thrombotic Events and Aseptic Meningitis Syndrome)<br>-Addition of interim safety analysis (March 2014) summary, which revealed no additional safety issue<br>-Deletion of inclusion criterion #2, reducing the length of time required for pre-study IVIG to 8 weeks<br>-Addition of Screening Period details: assessments could now be performed over > 1 visit; eligibility had to be determined before Screening efficacy measurements were performed and Screening IVIG was administered |
| 08 December 2015 | -Adverse reactions and precautions were updated per current safety information for IgPro10 (Transfusion-related Acute Lung Injury)<br>-Definition of "CIDP relapse" was clarified to be applicable to IgPro10 Restabilization as well as when it occurs during the SC Treatment Period |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

For endpoint, "Time to CIDP relapse or withdrawal due to any other reason during the SC treatment period (ITTS)", for the Placebo group the median time was 79.0 days (95% CI: 57.0 to 125.0). Other median times could not be calculated.

Notes: